

States with identical steady dissipation rate: Role of kinetic constants in enzyme catalysis

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Abstract

A non-equilibrium steady state is characterized by a non-zero steady dissipation rate. Chemical reaction systems under suitable conditions may generate such states. We propose here a method that is able to distinguish states with identical values of the steady dissipation rate. This necessitates a study of the variation of the entropy production rate with the experimentally observable reaction rate in regions close to the steady states. As an exactly-solvable test case, we choose the problem of enzyme catalysis. Link of the total entropy production with the enzyme efficiency is also established, offering a desirable connection with the inherent irreversibility of the process. The chief outcomes are finally noted in a more general reaction network with numerical demonstrations.

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1 Introduction

A major shift in the field of thermodynamics in the last century was from idealized equilibrium processes to natural irreversible processes [1-4]. Chemical reactions continue to play a pivotal role in this development and provide significant motivation in studying the non-equilibrium thermodynamic properties of systems *in vitro* as well as *in vivo* [5-10]. Since a closed system always tends to thermodynamic equilibrium (TE), a natural generalization in the theory of irreversible thermodynamics has been achieved via the concept of a steady state [1, 11]. In this regard, the quantity of primary importance is the entropy production rate (EPR) [12, 13, 14]. The EPR vanishes for a

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closed system in the long-time limit that reaches a true TE. On the other hand, EPR is positive definite for a steady state that can emerge in an *open* system. The easiest way to model such a system in the context of chemical reactions is to assume that concentrations of some of the reacting species are held fixed [15, 16]. Under this condition, aptly known as the chemiostatic condition [17], EPR tends to a non-zero constant, reflecting a steady dissipation rate (SDR) to sustain the system away from equilibrium [18]. The corresponding steady state is denoted as the non-equilibrium steady state (NESS) [19, 20, 21, 22]. This concept has been extensively used in analyzing single-molecule kinetic experiments [16, 17, 23]. The NESS also includes the TE as a special case when detailed balance (DB) is obeyed [24], thus providing a very general framework.

Recently, an important progress was made in the theory and characterization of NESS, considering a master equation formalism [25, 26, 27]. These studies have established that the classification of NESS requires *not only* the steady distribution (as in TE) but *also* the stationary fluxes or probability currents. This approach enables one to identify *all possible* combinations of transition rates that ultimately lead the system to the *same* NESS. However, these NESSs in general have different values of the EPR, and hence the SDR.

This proposition prompts one to check (i) how states with the same EPR at NESS can be generated and (ii) whether there exist ways to distinguish these states. Here, we shall address both the issues by considering an enzyme-catalyzed reaction under chemiostatic condition. Expressing the EPR as a function of experimentally measurable reaction rate, we emphasize also that, the quantity that identifies the various NESSs having the same EPR is linked with the enzyme efficiency, a useful measure that is expressible in terms of enzyme kinetic constants.

2 The system

The basic scheme of enzyme catalysis within the Michaelis-Menten (MM) framework with reversible product formation step is shown in Fig.1. Under chemiostatic condition, [S] and [P] are kept constant by continuous injection and withdrawal, respectively. This is the simplest model to mimic an open reaction system. Unlike the usual case of full enzyme recovery with total conversion of substrate into product in a closed system, here both the concentrations of free enzyme E and the enzyme-substrate complex ES reach a

steady value. Also, instead of the rate of product formation, the progress of reaction is characterized by the rate of evolution of $[E]$ (or $[ES]$).

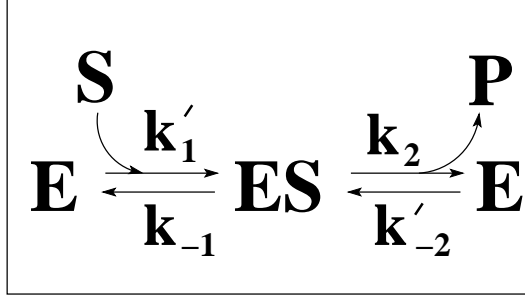


Figure 1: Schematic diagram of MM kinetics of enzyme catalysis with reversible product formation step under chemiostatic condition.

2.1 Kinetics

We define the pseudo-first-order rate constants as $k_1 = k'_1[S]$ and $k_{-2} = k'_{-2}[P]$. Concentration of **E** is denoted by $c_1(t)$ and that of **ES** is given by $c_2(t)$. We have then

$$c_1(t) + c_2(t) = z. \quad (1)$$

Here z is a constant that stands for the total enzyme concentration. Then the rate of the reaction, $v(t)$, is written as

$$v(t) = \dot{c}_1 = -Kc_1(t) + (k_{-1} + k_2)z, \quad (2)$$

where $K = (k_1 + k_{-1} + k_2 + k_{-2})$. With the initial condition, $c_1(0) = z$, the time-dependent solution is given as

$$c_1(t) = \frac{z}{K} \left((k_{-1} + k_2) + (k_1 + k_{-2})e^{-Kt} \right). \quad (3)$$

The steady state enzyme concentration corresponds to the long-time limit of Eq.(3):

$$c_1^s = ((k_{-1} + k_2)z) / K. \quad (4)$$

At any steady state, we thus note

$$v(t) = \dot{c}_1 = 0 = \dot{c}_2. \quad (5)$$

2.2 Non-equilibrium thermodynamics

The fluxes of the reaction system are defined pairwise as [2, 13, 14]

$$J_1(t) = k_1 c_1(t) - k_{-1} c_2(t), \quad (6)$$

$$J_2(t) = k_2 c_2(t) - k_{-2} c_1(t). \quad (7)$$

From Eq.(1), Eq.(2), Eq.(6) and Eq.(7), one gets

$$\dot{c}_1 = J_2(t) - J_1(t). \quad (8)$$

At the steady state, Eq.(8) leads to

$$J_1^s = J_2^s = J^s. \quad (9)$$

An NESS is characterized by a non-zero flux, $J^s \neq 0$. At TE, the fluxes vanish for both the reactions. One may note, then the system satisfies DB.

The conjugate forces of the fluxes given in Eqs (6)-(7) are defined as [2]

$$X_1(t) = \mu_E + \mu_S - \mu_{ES} = T \ln \frac{k_1 c_1(t)}{k_{-1} c_2(t)}, \quad (10)$$

$$X_2(t) = \mu_{ES} - \mu_E - \mu_P = T \ln \frac{k_2 c_2(t)}{k_{-2} c_1(t)}. \quad (11)$$

Corresponding to the scheme depicted in Fig.1, the EPR is then given by [1, 2]

$$\sigma(t) = \frac{1}{T} \sum_{i=1}^2 J_i(t) X_i(t). \quad (12)$$

We set here (and henceforth) the Boltzmann constant $k_B = 1$. In the present case, the steady value of EPR becomes

$$\sigma^s = \frac{1}{T} J^s (\mu_S - \mu_P). \quad (13)$$

Therefore, unless the substrate and the product take part in equilibrium, the reaction system reaches an NESS with a SDR equal to σ^s .

3 EPR close to NESS

The problem is now transparent. If the rate constants become different, the steady concentrations will also differ. But, one can adjust them in such a way that σ^s remains the same. In these situations, one needs an additional parameter to distinguish these states. To proceed, we define a small deviation in $c_1(t)$ around NESS as

$$\delta = c_1(t) - c_1^s. \quad (14)$$

It then follows from Eq.(1) that

$$c_2(t) = c_2^s - \delta. \quad (15)$$

From Eq.(2) and Eq.(14), the reaction rate becomes

$$v(t) = -K\delta. \quad (16)$$

Now, putting Eqs (6)-(11) and Eqs (14)-(16) in Eq.(12) and taking only the first terms of the logarithmic parts, we obtain the EPR close to NESS as

$$\sigma(t) = A_0 + A_1 v(t) + A_2 v^2(t). \quad (17)$$

Here

$$A_0 = J^s \ln \frac{k_1 k_2}{k_{-1} k_{-2}}, \quad (18)$$

$$A_1 = -\frac{1}{K} \left((k_1 + k_{-1}) \ln \frac{k_1 c_1^s}{k_{-1} c_2^s} + (k_2 + k_{-2}) \ln \frac{k_{-2} c_1^s}{k_2 c_2^s} \right), \quad (19)$$

$$A_2 = \frac{1}{K} \left(\frac{1}{c_1^s} + \frac{1}{c_2^s} \right). \quad (20)$$

As $v(t)$ vanishes at any steady state, the SDR at NESS is given by

$$\sigma^s = A_0 > 0. \quad (21)$$

However, at TE,

$$\sigma^s = A_0 = 0; \quad (22)$$

one may check that here DB holds:

$$\frac{k_1 k_2}{k_{-1} k_{-2}} = 1. \quad (23)$$

Inspection of Eq.(17) reveals that, near NESS, $\sigma(t)$ varies *linearly* with $v(t)$ with a slope A_1 . Thus, while A_0 distinguishes an NESS from a true TE, A_1 plays the same role in identifying systems with the *same* SDR but having *different* time profiles.

4 Results and discussion

In this section, we consider various situations where the reaction system reaches NESS with the same SDR. Focusing on Eq.(18), the different cases that keep A_0 invariant are discussed next.

4.1 Variants with same SDR

Case A: Any parent choice of rate constants.

Case B: Only k_1 and k_2 are exchanged.

Case C: Only k_{-1} and k_{-2} are exchanged.

Case D: Both k_1, k_2 and k_{-1}, k_{-2} are exchanged.

Case E: Both k_1, k_{-1} and k_2, k_{-2} are exchanged.

Case F: Both k_1, k_{-2} and k_2, k_{-1} are exchanged.

Case G: k_1 changed to αk_1 , k_{-1} changed to αk_{-1} , k_2 changed to βk_2 and k_{-2} changed to βk_{-2} , such that

$$\beta = \frac{1}{\alpha} = \frac{k_1 + k_{-1}}{k_2 + k_{-2}}.$$

It can be easily verified that cases D and E possess not only identical A_0 but also the same A_1 and A_2 . This is true for cases A and F as well. So, we do not consider cases E and F any further. A simple explanation of the equivalence is given in Fig.2 schematically, based on reflection symmetry.

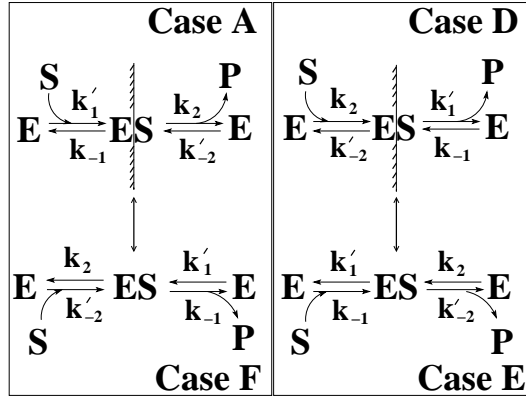


Figure 2: Schematic diagram showing the equivalence of the pairs A and F, and D and E, based on reflection symmetry.

4.2 Temporal profiles

To explore the characteristics of various cases given above, we take the rate constants from the single molecule experimental study of English *et al.* [23] on the *Escherichia coli* β -galactosidase enzyme. They are as follows: $k'_1 = 5.0 \text{ E07 M}^{-1}\text{s}^{-1}$, $k_{-1} = 1.83 \text{ E04 s}^{-1}$, $k_2 = 7.3 \text{ E02 s}^{-1}$. We clarify that, in their study [23], k_2 had actually been shown to be a fluctuating quantity with a distribution. However, only an *average* value of k_2 will suffice our purpose. The constant substrate concentration is set at $[S] = 1.0 \text{ E02 } \mu\text{M}$ and thus, $k_1 = k'_1[S] = 5.0 \text{ E03 s}^{-1}$. We choose $k_{-2} = 1.0 \text{ E-05 s}^{-1}$ to make the reaction scheme almost identical to the conventional MM kinetics. Here $\{k_i\}$ ($i = \pm 1, \pm 2$) with magnitudes given above represents the parent choice of rate constants, *i.e.*, case A. The value of the constant $\beta = 1/\alpha = 3.2 \text{ E01}$, in case G.

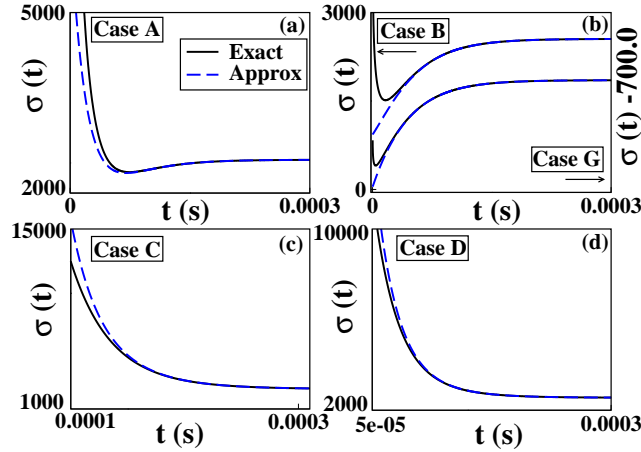


Figure 3: Evolution of EPR $\sigma(t)$ with time for various cases determined using the exact (Eq.(12)) as well as the approximate (Eq.(17)) expressions. In panel (b), the EPR of case G is plotted as $(\sigma(t) - 700.0)$ for clarity.

The time-evolution of EPR $\sigma(t)$, determined using both the exact (Eq.(12)) and the approximate (Eq.(17)) expressions, are shown in Fig.3, for the various cases. The concentrations c_1 , c_2 are made dimensionless by scaling with respect to the total enzyme concentration z . This ensures that $\sigma(t)$ has the unit of s^{-1} . From the figure, it is evident that Eq.(17) nicely approximates

the behavior near NESS. Specifically, the curves of exact and approximate cases merge quite well for any $t \geq 1.5 \text{ E-04 s}$.

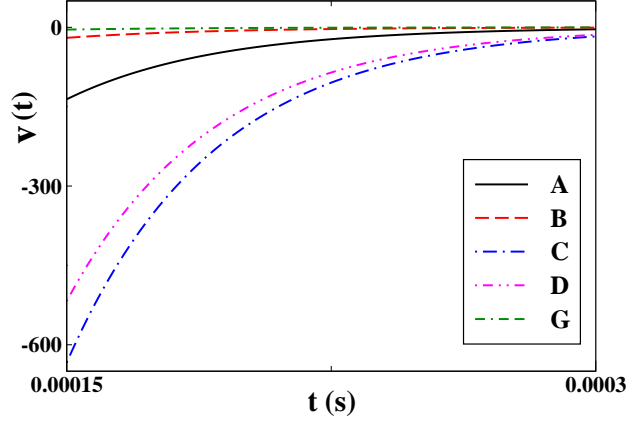


Figure 4: Variation of reaction rate $v(t)$ as a function of time for different cases indicated in the plot.

The evolution of reaction rate $v(t)$ is shown in Fig.4 for all the distinct cases. The curves are displayed over a time-span where Eq.(17) is valid, as mentioned above. This gives us a quantitative understanding of the magnitude of $v(t)$ up to which the *close to* NESS approximation, and hence Eq.(17), is valid. We note the variation of $\sigma(t)$ as a function of $v(t)$ in all the relevant cases in Fig.5. Both the exact (Fig.5(a)) as well as the approximate results (Fig.5(b)) are shown. Two features are interesting. First, in all the situations, the system reaches an NESS with identical $\sigma^s = A_0 = 2.553 \text{ E03 s}^{-1}$. Secondly, the quantity that distinguishes one case from the other is the slope A_1 of $\sigma(t)$ vs. $v(t)$ curve near the NESS. This slope can be positive as well as negative.

4.3 Total entropy production and enzyme efficiency

One may like to next investigate the role of the rate constants in governing the overall dissipation in various cases. Specifically, we like to enquire if the efficiency of the enzyme has anything to do with the total dissipation. In this

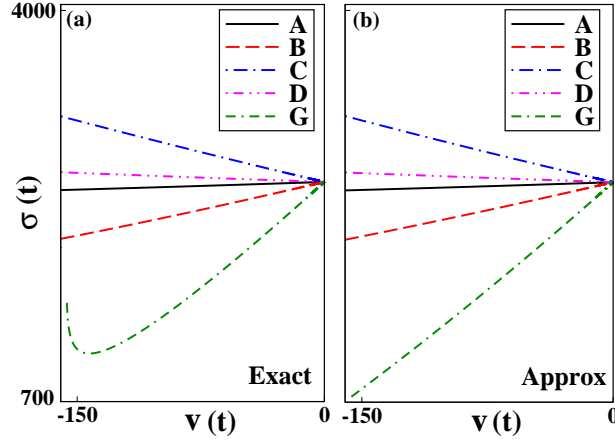


Figure 5: Variation of EPR $\sigma(t)$ as a function of reaction rate $v(t)$ for different cases indicated in the plot using (a) exact (Eq.(12)) and (b) approximate (Eq.(17)) expressions.

context, it may be recalled that, the conventional MM kinetics requires the rate constant k_{-2} to be negligible compared with the others. So, the enzyme kinetic constants, like the MM constant $K_M = \frac{k_{-1}+k_2}{k_1}$ and catalytic efficiency $\eta = k_2/K_M$, are meaningful in the limit $k_{-2} \rightarrow 0$. Our choice of parent rate constants ensures that in case A, the system follows MM kinetics. Case B, which leaves k_{-2} unchanged and case G, which changes k_{-2} to βk_{-2} (with $\beta = 3.2 \text{ E}01$), can also be included within the MM scheme. But, cases C to F, which exchange k_{-2} with any one of the other bigger rate constants, can not follow the usual MM kinetics. Therefore, we focus on cases A,B and G in finding any possible connection between the kinetic constants of the enzyme and the total dissipation. While the SDR σ^s is the same for all of them, the time-integrated EPR, giving the total entropy production, is different. We define it as

$$S_I = \int_0^\tau \sigma(t) dt. \quad (24)$$

The upper limit τ is fixed at such a time when all the systems reach NESS. In the present set of cases, we find that setting $\tau = 1.0 \text{ E-}03 \text{ s}$ is satisfactory. The values of K_M , η and S_I (determined by integrating $\sigma(t)$ from Eq.(12)) are listed in Table 1, along with the slope A_1 [see Eq.(17)]. It is clear from the

data that, in going from case A to case G, K_M gradually increases, whereas η falls. Both these features indicate that the enzyme becomes *less efficient*. More interesting is to note that the corresponding S_I values also exhibit a decreasing trend from case A to case G. Thus, we can say that, with identical SDR, the more efficient enzyme (bigger η and smaller K_M) involves higher *total* dissipation. This can be rationalized by the fact that, higher efficiency corresponds to a *faster* conversion of substrate into product. This implies an increased irreversibility in the process. Consequently, a higher entropy production is noted.

Table 1: Values of the quantities A_1 , K_M , η and S_I for cases A,B and G.

Case	A_1	K_M	η	S_I
A	4.715 E-01	3.806 E-04	1.918 E06	2.68 E0
B	3.256 E0	3.192 E-03	1.566 E06	2.48 E0
G	1.257 E01	1.524 E-02	1.529 E06	2.47 E0

Before ending this section, we mention briefly the fate of the different situations when DB, Eq.(23), gets satisfied. In this scenario, whatever be the values of the rate constants, the final EPR is trivially zero as the reaction system reaches TE [see Eq.(22)]. For the same reason, A_1 also becomes zero [see Eq.(19)]. However, it follows from Eq.(17) that, EPR varies *quadratically* with $v(t)$ near TE. Then, in principle, A_2 *can* distinguish systems reaching TE. It is easy to see from Eq.(20) that, cases A, B and G possess different values for A_2 and hence they can be identified by following the behavior of EPR with the reaction rate.

5 Extension to general reaction systems

The MM kinetics, shown in Fig.1, with a single intermediate in the form of the ES complex, is *exactly* solvable. We now generalize this scheme to an enzyme catalysis reaction having N number of species. These include the free enzyme E and (N-1) intermediates, under similar chemiostatic condition as discussed in Section II. The reaction scheme is depicted in Fig.6. Essentially, the species ES_j , ($j = 1, \dots, N - 1$) refer to the various conformers of the

enzyme-substrate complex. The corresponding rate equations are given as

$$\dot{c}_i = -(k_i + k_{-(i-1)})c_i(t) + k_{i-1}c_{i-1}(t) + k_{-i}c_{i+1}(t), \quad (25)$$

with $c_i(t)$ ($i = 1, \dots, N$) being the concentration of species $ES_{(i-1)}$ at time t . The following periodic boundary conditions hold:

$$i - 1 = N, \text{ for } i = 1,$$

$$i + 1 = 1, \text{ for } i = N.$$

We have set $k_1 = k'_1[S]$ and $k_{-N} = k'_{-N}[P]$. The flux J_i due to the i -th reaction is defined as

$$J_i(t) = k_i c_i(t) - k_{-i} c_{i+1}(t). \quad (26)$$

The expression of EPR then becomes

$$\sigma_N(t) = \sum_{i=1}^N J_i(t) \ln \frac{k_i c_i(t)}{k_{-i} c_{i+1}(t)}. \quad (27)$$

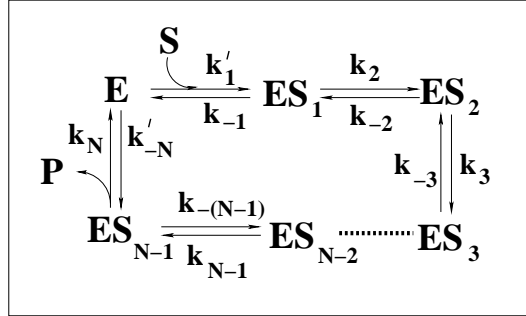


Figure 6: Schematic diagram of enzyme kinetics with $(N-1)$ number of intermediates under chemiostatic condition.

5.1 EPR as a functional of reaction rate near NESS

It is generally not possible to solve the set of coupled equations analytically for a system of arbitrary size. However, again focusing on a situation close to the NESS, one can get some insights. For that purpose, we define small deviations in species concentrations from their respective NESS values as

$$\delta_i(t) = c_i(t) - c_i^s. \quad (28)$$

For a short time interval τ , using finite difference approximation, one gets

$$\dot{\delta}_i = \dot{c}_i \approx \delta_i/\tau. \quad (29)$$

Putting Eqs (28)-(29) in Eq.(25), we get

$$\left(1 - (k_i + k_{-(i-1)})\tau\right) \delta_i(t) + k_{i-1}\tau\delta_{i-1}(t) + k_{-i}\tau\delta_{i+1}(t) = 0. \quad (30)$$

As the reactions are coupled, so the δ_i s are related to each other and can be expressed in terms of any one of them, say δ_1 . Then, one can write

$$\delta_i = f_i\delta_1, \quad \text{with } f_1 = 1. \quad (31)$$

Next we will discuss the scheme to determine the f_i s.

The set of coupled equations (30), with the help of Eq.(31), can be cast in the matrix form

$$\mathbf{M}\mathbf{f} = \mathbf{0}. \quad (32)$$

Here \mathbf{f} is a $N \times 1$ matrix with $\mathbf{f}^T = (f_1, f_2, \dots, f_N)$ and \mathbf{M} is a $N \times N$ matrix with the property

$$\begin{aligned} M_{ij} &\neq 0, \text{ for } j = i, i-1, i+1 \\ M_{ij} &= 0, \text{ otherwise.} \end{aligned} \quad (33)$$

The non-zero matrix elements are

$$M_{ii} = \left(1 - (k_i + k_{-(i-1)})\tau\right), \quad (34)$$

$$M_{i,i-1} = k_{i-1}\tau, \quad (35)$$

$$M_{i,i+1} = k_{-i}\tau. \quad (36)$$

From Eq.(32) and Eq.(33), we obtain a recursion relation

$$f_j = -\frac{(M_{j-1,j-2}f_{j-2} + M_{j-1,j-1}f_{j-1})}{M_{j-1,j}}, \quad j = 2, 3, \dots, N, \quad (37)$$

with the boundary conditions:

$$f_0 = f_N, \quad M_{j,0} = M_{j,N}.$$

The first of the relations becomes

$$f_2 = -\frac{M_{1N}f_N + M_{11}}{M_{12}}. \quad (38)$$

Then, it is easy to follow from Eq.(37) that, all the other f_j s can be expressed in terms of f_N . From the condition

$$\sum_{i=1}^N c_i = \text{constant}, \quad (39)$$

we get

$$\sum_{i=1}^N \delta_i = 0, \quad (40)$$

and using Eq.(31), we have

$$\sum_{i=2}^N f_i = -1. \quad (41)$$

From Eqs (34)-(38) and Eq.(41), one can determine the f_i s in Eq.(31).

We are now ready to explore the EPR near the NESS. From Eq.(25), we have

$$J_i^s = J^s, \quad (i = 1, \dots, N) \quad (42)$$

at NESS. As we have chosen to express all the deviations in concentration from the NESS in terms of δ_1 , so we take the reaction rate as $v(t) = \dot{a}_1$. Then, from Eq.(25) with $i = 1$ and using Eq.(31) along with the periodic boundary conditions, we get near NESS

$$v(t) = R\delta_1, \quad (43)$$

where

$$R = -(k_1 + k_{-N}) + k_N f_N + k_{-1} f_2. \quad (44)$$

Now putting Eq.(28), Eq.(31), Eq.(42) and Eq.(43) in Eq.(27) and also using the smallness of δ_i s, the EPR near NESS becomes

$$\begin{aligned} \sigma_N(t) &= \sum_{i=1}^N (J^s + k_i \delta_i - k_{-i} \delta_{i+1}) \left(\ln \frac{k_i c_i^s}{k_{-i} c_{i+1}^s} + \frac{\delta_i}{c_i^s} - \frac{\delta_{i+1}}{c_{i+1}^s} \right) \\ \sigma_N(t) &= A_N^{(0)} + A_N^{(1)} v(t) + A_N^{(2)} v^2(t), \end{aligned} \quad (45)$$

with

$$A_N^{(0)} = J^s \ln \frac{\prod_{i=1}^N k_i}{\prod_{i=1}^N k_{-i}}, \quad (46)$$

$$A_N^{(1)} = \frac{1}{R} \sum_{i=1}^N (k_i f_i - k_{-i} f_{i+1}) \ln \frac{k_i c_i^s}{k_{-i} c_{i+1}^s}, \quad (47)$$

$$A_N^{(2)} = \frac{1}{R^2} \sum_{i=1}^N (k_i f_i - k_{-i} f_{i+1}) \left(\frac{f_i}{c_i^s} - \frac{f_{i+1}}{c_{i+1}^s} \right). \quad (48)$$

Eq.(45) is the generalized version of Eq.(17), confirming that expression of the EPR as a functional of reaction rate possesses a universal character.

5.2 Cases with invariant SDR

The next task is, whether states having the same SDR, *i.e.*, identical $A_N^{(0)}$, can be generated for the N-cycle. An obvious clue comes from the invariance of a cycle under rotation. Thus, if the steady concentrations c_i^s are represented as N points uniformly placed on a circle, then rotations by an angle θ , defined as

$$\theta = \frac{2\pi j}{N}, \quad j = 1, \dots, (N-1), \quad (49)$$

will just redistribute the c_i^s values. This keeps the steady flux J^s in Eq.(46) unchanged. Therefore, for a N-cycle, there are *at least* (N-1) ways to interchange the rate constants $k_{\pm i}$ that will lead the reaction system to states with the same SDR. We illustrate this result here by taking the simplest non-trivial case of a triangular network as an example.

One can see from Eq.(49) that, for a triangular network with $N = 3$, *at least* two kinds of changes of the rate constants keep the SDR unchanged. They are given below:

Case 1. Any parent choice of rate constants.

Case 2. Change $k_{\pm i} \rightarrow k_{\pm(i+1)}$, ($i = 1, \dots, N$) with the boundary condition $k_{\pm(N+1)} = k_{\pm 1}$.

Case 3. Change $k_{\pm 1} \rightarrow k_{\pm 3}$, $k_{\pm 2} \rightarrow k_{\pm 1}$ and $k_{\pm 3} \rightarrow k_{\pm 2}$.

One can generate additional ways to keep $A_N^{(0)}$ fixed with some added constraints on the rate constants. Two pairs of situations [cases 4 and 5, and 6 and 7] are the following:

Case 4. Any parent choice of rate constants with $k_1 = k_{-1}$.

Case 5. Change $k_1 \rightarrow k_2$, $k_2 \rightarrow k_3$, $k_3 \rightarrow k_{-1}$, $k_{-1} \rightarrow k_{-2}$, $k_{-2} \rightarrow k_{-3}$ and $k_{-3} \rightarrow k_1$.

Case 6. Any parent choice of rate constants with $k_3 = k_{-3}$.

Case 7. Change $k_1 \rightarrow k_{-3}$, $k_{-3} \rightarrow k_{-2}$, $k_{-2} \rightarrow k_{-1}$, $k_{-1} \rightarrow k_3$, $k_3 \rightarrow k_2$ and $k_2 \rightarrow k_1$.

All the above variants have been numerically studied and shown in Fig.7 where the EPR, determined exactly by Eq.(27), is plotted as a function of

reaction rate $v(t) = a_1$ for each of the cases. It is evident from the figure that the SDR are identical for the respective bunch of cases. But they can be distinguished by following the $\sigma_3(t)$ vs. $v(t)$ curve in the small- $v(t)$ regime.

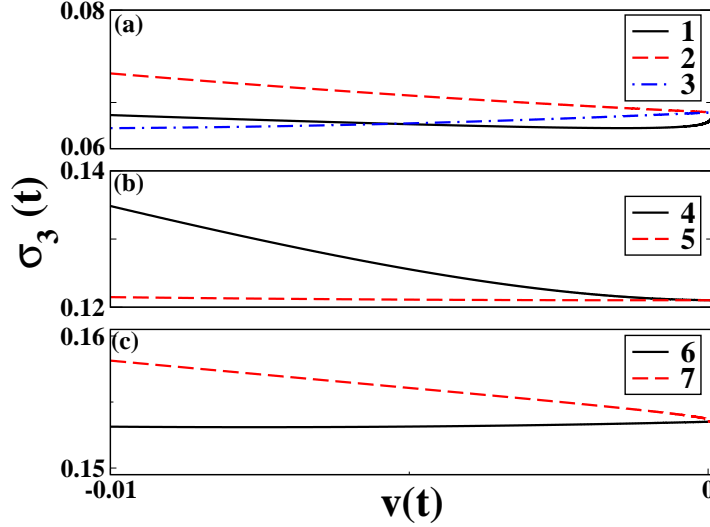


Figure 7: Variation of EPR $\sigma_3(t)$ (Eq.(27)) as a function of reaction rate $v(t)$ for cases (a) 1,2 and 3, (b) 4 and 5, (c) 6 and 7.

6 Conclusion

In summary, the present endeavor has been to characterize steady states with the same non-zero SDR. We have found that the variation of EPR with the reaction rate near completion of the reaction is a nice indicator to distinguish such states. Particularly important is the role of the slope of $\sigma(t)$ vs. $v(t)$ curve near $v(t) = 0$. This has been substantiated by studying enzyme-catalysed reactions as an exactly-solvable test case. We have also noticed, the leading term that accounts for the variation depends on the rate constants, more specifically on the enzyme efficiency. It is gratifying to observe that the more efficient enzyme incurs higher total dissipation. The physical appeal is immediate. A more efficient enzyme approaches the steady state more quickly. This implies the process becomes more irreversible. Hence, S_I

becomes higher. One more notable point is the following. The SDR is equal to the steady heat dissipation rate. Our study reveals that enzymes with very different efficiencies can show the same heat dissipation rate at steady state. An extension to cases of higher complexities involving various conformers of the enzyme-substrate complex has also been envisaged. Further studies along this line on enzymes with multiple sites may be worthwhile.

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